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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,152	08/04/2006	James Peter Burnie	22083-008US1 / WA/MC/MP10	8989

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EXAMINER	
SWARTZ, RODNEY P	
ART UNIT	PAPER NUMBER
1645	

NOTIFICATION DATE	DELIVERY MODE
09/29/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATDOCTC@fr.com

Office Action Summary	Application No.	Applicant(s)	
	10/553,152	BURNIE ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *40* is/are allowed.

6)☒ Claim(s) *19-39-41-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 22 August 2008 has been entered.

Claims 22, 26, and 33 have been amended. New claims 40-43 have been added.

2. Claims 19-43 are pending and under consideration.

Rejections Withdrawn

3. The rejection of claim 26 under 35 U.S.C. 112, second paragraph, as being indefinite for "pronounced" antibody response, is withdrawn in light of the amendment of the claim.

4. The rejection of claim 33 under 35 U.S.C. 112, second paragraph, as being indefinite for antibodies "not effective", is withdrawn in light of the amendment of the claim.

Rejections Maintained

5. The provisional rejection of claims 19, 20, 21 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 13 and 15 of copending Application No. 11/630,926 is maintained.

Applicants request deferral of the issue until there is allowable matter.

6. The rejection of claims 22-36 under 35 U.S.C. 112, second paragraph, as being indefinite for antibodies "specific against at least one antigen", is maintained.

Applicants argue that the claims are definite in that it is clear that sequences identified and the antibodies generated using the method of amended claim 22 are specific against at

least one antigen of *C. difficile*. In addition, claim 22 has been amended to recite "confirming that an antibody comprising the dominant sequence is therapeutically effective".

The examiner has considered applicants' arguments, in light of the amendment of claim 22, but does not find them persuasive.

Newly amended claim 22 is drawn to a method for identifying candidate antigen-specific sequences of antibodies specific against at least one antigen produced by *C. difficile* comprising: (i) obtaining B cells from at least one patient whose immune system has been exposed to the antigen and sequencing from the B-cells at least CDR3 regions of VH or VL, or both, (ii) detecting a set of sequences that occur in total at a frequency of at least one percent wherein the set of sequences include a dominant sequence and sequences of at least 80% homology to the dominant sequence, and (iii) confirming that an antibody comprising the dominant sequence is therapeutically effective.

While the claim does determine sequences that occur in total at a frequency of at least one percent, it is unclear how one determines that the antibodies are "specific against at least one antigen" of *C. difficile*. In step (i), one collects all B-cells, not just B-cells which may interact with a *C. difficile* antigen. Thus, the B-cell population is a heterologous population, containing cells reactive to any number of unknown moieties. In step (ii), the only criterion for selection is a frequency of $\geq$1% for CDR3 regions of VH or VL or both. There is no restriction to the reactivity of the regions. Thus, if the patient was currently in an active B-cell immune response to any other moiety, these CDR3 regions would probably meet the only criterion for selection. In step (iii), there is no restriction on what the antibody is "therapeutically effective" against. Again, this permits selection of non-*C. difficile* antibodies.

Therefore, the claims remain indefinite concerning the ability to distinguish between *C. difficile* antibodies and antibodies against any other moiety.

7. The rejection of claims 37-39 under 35 U.S.C. 112, second paragraph, as being indefinite for dependence from rejected claims, is maintained.

Claim Objections

8. Claim 41 is objected to because of the following informality: there should be an "and" between steps i and ii. Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claim 41 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to a method for identifying candidate antigen-specific sequences of antibodies specific against at least one antigen produced by *C. difficile* comprising: (i) obtaining B cells from two or more patients whose immune systems have been exposed to the antigen and sequencing from the B-cells from both patients at least CDR3 regions of VH or VL, or both; and, (ii) detecting a set of sequences that occur in the two or more patients in total at a frequency of at least one percent wherein the set of sequences include a dominant sequence and sequences of at least 80% homology to the dominant sequence, and wherein the detection of the set of sequences in the two or more patients confirms that the set of sequences is specific against *C. difficile*.

While the claim may determine sequences that occur in two or more patients in total at a frequency of at least one percent, it is unclear how one determines that the antibodies are "specific against at least one antigen" of *C. difficile*. In step (i), one collects all B-cells, not just B-cells which may interact with a *C. difficile* antigen. Thus, the B-cell population is a heterologous population, containing cells reactive to any number of unknown moieties. In step (ii), the only criterion for selection is a frequency of $\geq$1% for CDR3 regions of VH or VL or both. There is no restriction to the reactivity of the regions. Thus, if both of the patients were currently in an active B-cell immune response to another moiety, these CDR3 regions would probably meet the only criterion for selection. This permits selection of non-*C. difficile* antibodies. Therefore, the claim is unclear how one distinguishes between *C. difficile* antibodies and antibodies against any other moiety.

11. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to a method for identifying candidate antigen-specific sequences of antibodies specific against at least one antigen produced by *C. difficile* comprising: (i) obtaining B cells from at least one patient whose immune system has been exposed to the antigen and sequencing from the B-cells at least CDR3 regions of VH or VL, or both, (ii) comparing the sequences of step (i) with sequences of least CDR3 regions of VH or VL, or both, from a patient not exposed to said antigen, and (iii) detecting a set of sequences that occur in total at a frequency of at least one percent in the sequences identified in step (i) and at a frequency of less than one percent in the sequences from the non-exposed patient, wherein the set of

sequences include a dominant sequence and sequences of at least 80% homology to the dominant sequence.

While the claim does determine sequences that occur in total at a frequency of at least one percent in the exposed patient, but at a frequency of less than one percent in the sequences from the non-exposed patient, it is unclear how one determines that the antibodies are "specific against at least one antigen" of *C. difficile*. In step (i), one collects all B-cells, not just B-cells which may interact with a *C. difficile* antigen. Thus, the B-cell population is a heterologous population, containing cells reactive to any number of unknown moieties. In step (ii), the only criterion for selection is a frequency of $\geq$1% for CDR3 regions of VH or VL or both in an exposed patient, while the only criterion for selection is a frequency of <1% for CDR3 regions of VH or VL or both in a nonexposed patient There is no restriction to the reactivity of the regions. If the exposed patient was currently in an active B-cell immune response to any other moiety, these CDR3 regions would probably meet the only criterion for selection. Therefore, the claim is unclear how one distinguishes between *C. difficile* antibodies and antibodies against any other moiety.

12. Claim 43 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to a method for identifying candidate antigen-specific sequences of antibodies specific against at least one antigen produced by *C. difficile* comprising: (i) obtaining B cells from at least one patient prior to exposure to the antigen and sequencing from the B-cells at least CDR3 regions of VH or VL, or both, (ii) obtaining B cells from said patient after exposure to the antigen and sequencing from the B-cells at least CDR3 regions of VH or VL, or

both; and, (iii) detecting a set of sequences that occur in total at a frequency of at least one percent in the sequences identified in step (ii) and at an increased frequency with respect to the seqauences identified in step (i), wherein the set of sequences include a dominant sequence and sequences of at least 80% homology to the dominant sequence.

While the claim does determine sequences that occur in total at a frequency of at least one percent in the patient following exposure to the antigen, it is unclear how one determines that the antibodies are "specific against at least one antigen" of *C. difficile*. In both step (i) and step (ii), one collects all B-cells, not just B-cells which may interact with a *C. difficile* antigen. Thus, the B-cell population is a heterologous population, containing cells reactive to any number of unknown moieties. In step (iii), the only criterion for selection is a frequency of $\geq$1% in the sequences identified in step (ii) and at an increased frequency with respect to the sequences identified in step (i). There is no restriction to the reactivity of the regions. If the patient was simultaneously exposed to any other moiety at the time of exposure to said *C. difficile* antigen, these CDR3 regions would probably meet the only criterion for selection. Therefore, the claim is unclear how one distinguishes between *C. difficile* antibodies and antibodies against any other moiety.

Conclusion

13. Claims 19-39 and 41-43 are rejected.

14. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rodney P. Swartz, Ph.D., Art Unit 1645, whose telephone number is (571) 272-0865. The examiner can normally be reached on Monday through Wednesday from 9:00 AM to 7:30 PM EST. Thursday is the examiner's work at home day.

If attempts to reach the Examiner by telephone are unsuccessful, please contact the Examiner's Supervisors, Shannon Foley (571)272-0898, and Robert B. Mondesi (571)272-0956.

The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Rodney P. Swartz, Ph.D./

Primary Examiner, Art Unit 1645

September 25, 2008

Application Number	Application/Control No.	Applicant(s)/Patent under Reexamination	
	10/553,152	BURNIE ET AL.	
	Examiner	Art Unit	
	Rodney P. Swartz, Ph.D.	1645	